9 April 2013

Joint open letter by 11 European or International Organisations

Clinical Trials Regulation
Protect public health: Choose transparency!

Dear Member of the European Parliament,

As researchers, doctors, scientists, patients and civil society representatives we are asking you to support the inclusion of **strong transparency provisions** in the Clinical Trial Regulation that is currently being discussed.

In particular, we ask you to:

- **support amendments that require the public disclosure of a complete clinical study report (CSR)** as outlined by ENVI rapporteur MEP Glenis Willmott;
- **reject amendments strengthening the protection of so-called "commercially confidential" or "commercially sensitive" information** which would be a major step back and undermine the accountability of the European pharmaceutical regulation system.

An overriding public interest is at stake, namely public health. At present, **half of all clinical trials are never published.** Of those that are published, only a selection of positive results, from which important harms may have been omitted, are disclosed. This is a waste of research money and an abuse of clinical trial participants' altruism and trust (1 to 5).

Recent drug disasters (e.g. *rofecoxib* (Vioxx°), *rosiglitazone* (Avandia°), *rimonabant* (Acomplia°), etc.) occurred to such a large extent due to delayed decision-making at the regulatory level. On most occasions, regulators rely solely on the pharmaceutical company's analysis of their own products' benefit-harm balance (**a**) (6).

Numerous recent drug disasters would have been avoided if public access to clinical data had been granted. In fact, disclosing key information allows for **timely and independent data reanalysis** (scrutiny by the scientific community) and enables the public to act as a **watchdog** (public scrutiny of regulatory decisions) (3,7,8).

A summary of clinical trial results is insufficient. The scientific data generated in clinical trials data are a public good. Patients who take part do so in the hope that their contribution will benefit the advancement of science (1,2,4).

The disclosure of a summary of results, as suggested by the European Commission, is of little scientific value, as it does not supply healthcare professionals and independent researchers with the information they need to judge the merit of a trial or to be able to use its results to support rational prescribing.

The Helsinki Declaration requires authors to make the results of their research on human subjects publicly available, and to be accountable for the completeness and accuracy of their reports. A summary does not live up to these ethical requirements.

Access to all the data from clinical trials, in the form of clinical study reports, is crucial to ensure the reliability of pharmaceutical safety and efficacy data and to respect patients who participate in clinical trials.

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a- For example, despite the lack of evidence that *oseltamivir* (Tamiflu°) is effective in preventing the complications of influenza, EU governments stockpilled millions of doses of Tamiflu°, wasting billions of euros of taxpayers' money (ref. 8).

Disclosure of Clinical study reports' (CSR) helps to advance biomedical research. A recent study published in *BMJ open* has shown that **clinical study reports are comprehensive documents** of on average 1 800 pages, containing the following sections: report synopses (about 5 pages), efficacy evaluation (about 13 pages), safety evaluation (17 pages), trial protocol (about 60 pages), and the remaining pages are attached tables and anonymised individual efficacy and safety listings (8). Moreover, the European Ombudsman's ruling is that **clinical study reports contain no "commercially confidential" information** (2,7).

Science has to be reproducible and researchers are already ethically obliged to write a report under any circumstances. **Establishing clinical study reports (CSR) or a full dataset as a disclosure format does not represent an added burden for academics or non-commercial researchers.** Published clinical study results are increasingly published together with the full dataset of individual anonymised patients data: the researchers often simply upload the files containing their full dataset to the website of the publisher (9,10).

The submission and subsequent disclosure of complete reports in the EU Portal would greatly help the advancement of biomedical research and lead to more rational and better healthcare.

In brief: Transparency is key to ensure better patient care, today and tomorrow. The lack of complete information on the efficacy and safety of medicines causes significant harm to millions of citizens, stifles scientific progress and often leaves healthcare professionals in the dark concerning the medicines they choose to prescribe and dispense.

Recognising and enforcing transparency and access to information within the legal framework is an effective tool to promote both informed decision-making at the individual level and collective democratic participation.

We therefore count on your commitment, as Members of the European Parliament, to carry this message forward and support transparency.

Signatory organisations:

AGE Platform Europe
Association Internationale de la Mutualité (AIM)
Cochrane Collaboration
European AIDS Treatment Group (EATG)
European Social Insurance Platform (ESIP)
Health Action International (HAI) Europe
International Society of Drug Bulletins (ISDB)
Medicines in Europe Forum (MiEF)
PLOS Medicine
TransAtlantic Consumer Dialogue (TACD)
WEMOS

Individual signatories:

Trudo Lemmens, professor of law and bioethics, specialized in Health Law and Policy, particularly the regulation of pharmaceuticals (University of Toronto) (contact: trudo.lemmens@dph.ox.ac.uk)
Jim Murray, former director of the Bureau Européen des Unions de Consommateurs (BEUC) and editor of the blog http://openmedicineeu.blogactiv.eu (contact: openmedicine.eu@gmail.com)

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References:

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2- Gøtzsche PC, Jørgensen AW "Opening up data at the European Medicines Agency" BMJ 2011; 342:d2686 doi: 10.1136/bmj.d2686.
3- Wieseler B et al. (Institute for Quality and Efficiency in Health Care) "Access to regulatory data from the European Medicines Agency: the times they are a-changing" Systematic Reviews 2012, **1**:50 doi:10.1186/2046-4053-1-50 (http://www.systematicreviewsjournal.com/content/1/1/50)
4- Kmietowicz Z "Trial participants call for drug regulator to ensure study results are published" *BMJ 2013;346:f382*.
5- Vedula S, Li T and Dickersin K "Differences in reporting analyses in internal company documents versus published trial reports: comparisons in industry-sponsored trials in off-label uses of Gabapentin" *PLOS Med* 2013 ; **10** (1): 13 pages.
6- Prescrire Editorial Staff "How to avoid future *Vioxx*°-type scandals" *Prescrire* Int 2005; 14 (77): 115-117.
7- Several initiatives call for more transparency, for example "Ottawa Statement on trial registration" (http://ottawagroup.ohri.ca/disclosure.html) or the campaign and petition "All Trials Registered - All Results Reported" (www.alltrials.net).
8- Doshi P, Jefferson T "Clinical study reports of randomised controlled trials: an explanatory review of previously confidential industry reports" BMJ Open 2013; **3**: e002496. Doi: 10.1136/bmjopen-2012-002496.
9- http://bmjopen.bmj.com
10- An exemple is a recent study evaluating the association between bisphosphonate use and the risk of atypical femoral fractures among women aged 65 or older (http://datadryad.org/resource/doi:10.5061/dryad.h435m).

Signatory organisations

AGE Platform Europe is a European network of around 170 organisations of and for people aged 50+ which aims to voice and promote the interests of the 150 million senior citizens in the European Union and to raise awareness on the issues that concern them most. More information: www.age-platform.eu. Contact: Anne-Sophie Parent (Secretary General, annesophie.parent@age-platform.eu), Julia Wadoux (Policy Officer, julia.wadoux@age-platform.eu)

The Association Internationale de la Mutualité (AIM) is an organisation of autonomous health insurance and social protection bodies operating according to the principles of solidarity and non-profit-making. Currently, AIM's membership consists of 41 national federations representing 29 countries. In Europe, they provide social coverage against sickness and other risks to more than 150 million people. AIM strives via its network to make an active contribution to the preservation and improvement of access to health care for everyone. More information: www.aim-mutual.org. Contact: corinna.hartrampf@aim-mutual.org

The Cochrane Collaboration is an international not-for-profit international network of more than 28,000 dedicated people from over 100 countries preparing, maintaining and promoting the accessibility of systematic reviews of the effects of health care. More information: www.cochrane.org. Contact: Peter Gøtzsche (pcg@cochrane.dk)

The European AIDS Treatment Group (EATG) is a European network of nationally-based volunteer activists comprising of more than 110 members from 40 countries in Europe. EATG members are representatives of different communities affected by HIV/AIDS in Europe. More information: www.eatg.org. Contact: koen.block@eatg.org

European Social Insurance Platform (ESIP) represents a strategic alliance of over 40 statutory social security organisations in 15 EU Member States, Croatia and Switzerland. ESIP's mission is to preserve high profile social security for Europe, to reinforce solidarity based social insurance systems, and to maintain European social protection quality. More information: www.esip.org. Contact: esip@esip.org
Note: ESIP members support this position in so far as the subject matter lies within their field of competence.

Health Action International (HAI) is an independent global network of health, consumer and development organisations working to increase access to essential medicines and improve their rational use. More info: www.haieurope.org. Contact: tessel@haieurope.org

The International Society of Drug Bulletins (ISDB), founded in 1986, is a worldwide Network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of pharmaceutical industry. Currently ISDB has around 80 members in 41 countries around the world. More information: www.isdbweb.org. Contact: press@isdbweb.org

The Medicines in Europe Forum (MiEF) was launched in March 2002 and reaches 12 European Member States. It includes more than 70 member organisations representing the four key players on the health field, i.e. patients groups, family and consumer bodies, social security systems, and health professionals. Such a grouping is unique in the history of the European Union and is testament of the importance of European medicines policy. Contact: pierrechirac@aol.com

PLOS Medicine is the leading open-access medical journal, providing an influential venue for outstanding research and commentary on the major challenges to human health worldwide. PLOS Medicine specifically seeks to publish articles relevant to clinicians and policymakers across a range of settings that adhere to the highest standards of methodology, ethics and reporting and address the major biological, environmental, social, and political determinants of health. More information: www.plosmedicine.org. Contact: vbarbour@plos.org

The Transatlantic Consumer Dialogue (TACD) is a forum of US and EU consumer organisations which develops and agrees on joint consumer policy recommendations to the US government and European Union to promote the consumer interest in EU and US policy making. More information: www.tacd.org. Contact: tacd@consint.org or hammerstein.david3@gmail.com

Wemos. Wemos influences international policy in such a way that the right to health is respected, protected and promoted. In doing so, Wemos devotes special attention to vulnerable sections of society. Wemos advocates ethical conduct, coherent policy and equal access to care. Its lobbying work focuses on lasting improvements in Dutch, European and global policy. More information: www.wemos.nl. Contact: annelies.den.boer@wemos.nl